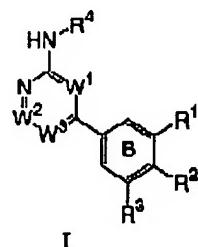


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AMENDMENTS TO THE CLAIMS

Please replace all prior versions and listings of claims with the amended claims as follows:

1. (Currently amended) A compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

W¹ is nitrogen or CH, W² is nitrogen or C-(U)_pR^U, and W³ is nitrogen or C-(V)_qR^V;

p and q are each independently 0 or 1;

R^U and R^V are each independently R or Ar^J;

U and V are each independently a bond or a C₁₋₆ alkylidene chain, wherein up to two methylene units of the chain are optionally and independently replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR;

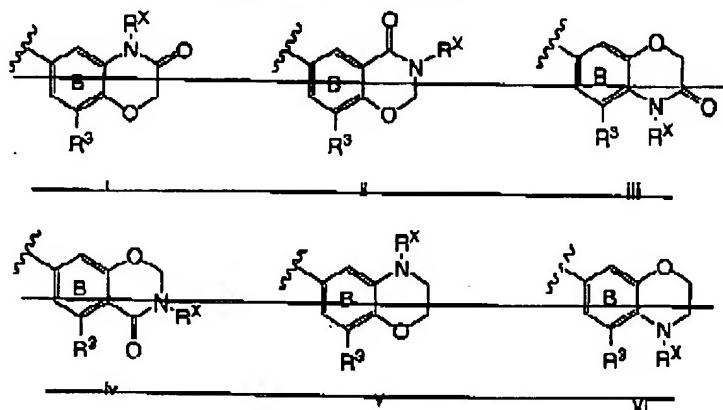
each occurrence of R is independently hydrogen or an optionally substituted C_{1-C4} aliphatic, or two R bound to the same nitrogen atom are optionally taken together with the nitrogen atom to form a 3-7 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Ar^J is a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-12 membered saturated, partially unsaturated, or fully unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or

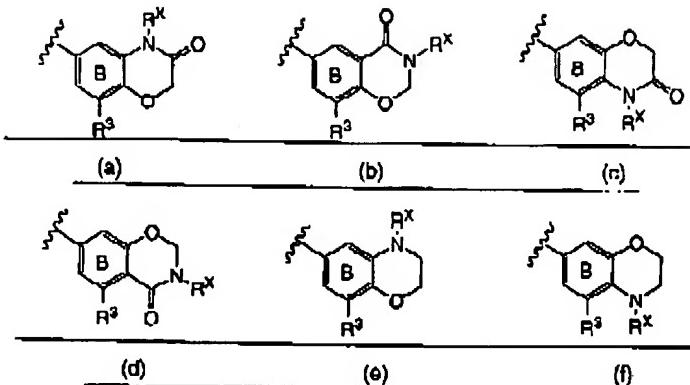
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sulfur; wherein Ax^1 is optionally substituted with m independent occurrences of $Z-R^5$; wherein m is 0-5, Z is a bond or is a C_1-C_6 alkylidene chain wherein up to two methylene units of Z are optionally replaced by CO , CO_2 , $COCO$, $CONR$, $OCONR$, $NRNR$, $NRNRCO$, $NRCO$, $NRCO_2$, $NRCONR$, SO , SO_2 , $NRSO_2$, SO_2NR , $NRSO_2NR$, O , S , or NR ; and each occurrence of R^5 is independently hydrogen, an optionally substituted aliphatic, heteroaliphatic, aryl or heteroaryl group, halogen, NO_2 , CN , OR , SR , $N(R)_2$, $NRCOR$, $NRCON(R)_2$, $NRCO_2R$, COR , CO_2R , $OCOR$, $CON(R)_2$, $OCON(R)_2$, SOR , SO_2R , $SO_2N(R)_2$, $NRSO_2R$, $NRSO_2N(R)_2$, $COCOR$, or $COCH_2COR$;

R^1 and R^2 are taken together and fused to ring B to form a cyclic heterocyclic moiety selected from one of the following formulae (a) through (f):



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wherein each occurrence of R^X is independently hydrogen, QR, or Q_nAr^1 ; n is zero or one; and Q is an optionally substituted C_{1-4} alkylidene chain wherein one methylene unit of Q is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR; R^3 is hydrogen, halogen, QR, Q_nCN , Q_nNO_2 , or Q_nAr^1 ; and R^4 is Ar^1 , or T-Ar¹; wherein T is a C_{1-2} alkylidene chain wherein one methylene unit of T is optionally replaced by CO, CO₂, COCO, CONR, OCONR, NRNR, NRNRCO, NRCO, NRCO₂, NRCONR, SO, SO₂, NRSO₂, SO₂NR, NRSO₂NR, O, S, or NR.

2. (Currently amended) The compound of claim 1, wherein R^1 and R^2 taken together represent heterocycle-i form the heterocyclic moiety of formula (a) and R^X is hydrogen or optionally substituted C_{1-6} aliphatic.
3. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C_{1-6} alkyl substituted with $N(R)_2$, or C_{1-6} alkyl substituted with Ar^1 .

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4. (Original) The compound of claim 1, wherein R^X is hydrogen, methyl, or C₁₋₃alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

5. (Original) The compound of claim 1, wherein R³ is hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 3-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur.

6. (Original) The compound of claim 1, wherein R³ is hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂, O(CH₂)₂NH(C₁₋₄ aliphatic), O(CH₂)₂N(C₁₋₄ aliphatic)₂, Br, Cl, or F.

7. (Original) The compound of claim 1, wherein R³ is hydrogen.

8. (Original) The compound of claim 1, wherein R⁴ is a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogen atoms, or a 5 membered heteroaryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each ring is optionally substituted.

9. (Original) The compound of claim 1, wherein R⁴ is optionally substituted phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl.

10. (Original) The compound of claim 1, wherein R⁴ is an optionally substituted phenyl group.

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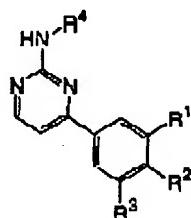
11. (Original) The compound of claim 8, wherein each occurrence of Z is independently a bond or a C₁₋₄ alkylidene chain wherein one methylene unit of Z is optionally replaced by -O-, -S-, -SO₂-, or -NH-; and each occurrence of R⁵ is independently hydrogen, C₁₋₆ aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, or pyrimidinyl.

12. (Currently amended) The compound of claim 8, wherein each occurrence of ZR⁷ is independently Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylene-di-oxo methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, ~~aminophenyl~~, phenyl, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, and fluorophenoxy.

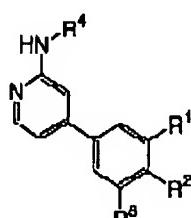
13. (Original) The compound of claim 1, wherein (U)_pR^U and (V)_qR^V are each independently hydrogen, halogen, NO₂, CN, OR, SR or N(R)₂, or C₁₋₄aliphatic optionally substituted with oxo, OR, SR, N(R)₂, halogen, NO₂ or CN.

14. (Original) The compound of claim 1, wherein (U)_pR^U and (V)_qR^V are each independently hydrogen, Me, OH, or OMe.

15. (Original) The compound of claim 1, wherein W¹ is N or CH and compounds have the structure of Formula Ia or Ib:



Ia

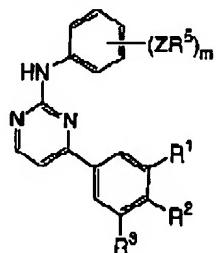


Ib

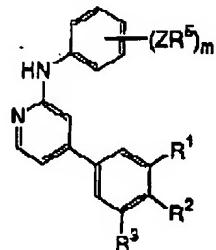
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or a pharmaceutically acceptable salt thereof.

16. (Currently amended) The compound of claim ([1]) 15, wherein R⁴ is an optionally substituted phenyl group and compounds have the structure of Formula IIa or IIb:



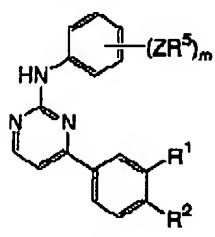
IIa



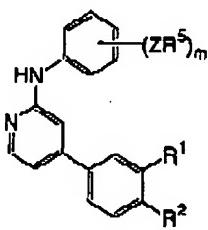
IIb

or a pharmaceutically acceptable salt thereof.

17. (Currently amended) The compound of claim ([1]) 16, wherein R³ is hydrogen, and compounds have the general structure of Formula IIIa or IIIb:



IIIa

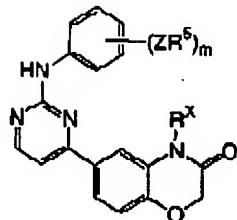


IIIb

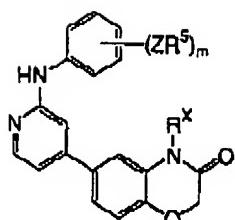
or a pharmaceutically acceptable salt thereof.

18. (Currently amended) The compound of claim ([1]) 16, wherein R³ is hydrogen, and R¹ and R² taken together represent the heterocycle form the heterocyclic moiety of formula (a) and compounds have the general structure of Formula IVa or IVb:

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IVa



IVb

or a pharmaceutically acceptable salt thereof.

19. (Currently amended) The compound of claim 15 of any one of claims 15, 16, 17 or 18, wherein

i) R¹ and R² taken together represent the heterocycle I depicted above form the heterocyclic moiety of formula (a); where R^X is defined according to one of the following groups:

- [(a.)] (a) hydrogen or optionally substituted C₁₋₄aliphatic;
- [(b.)] (b) hydrogen, methyl, ethyl, propyl, n-butyl, tert-butyl, pentyl, cyclopentyl, hexyl, cyclohexyl, C₁₋₆alkyl substituted with N(R)₂, or C₁₋₆alkyl substituted with Ar¹; or
- [(c.)] (c) hydrogen, methyl, or C₁₋₂alkyl substituted with a group selected from optionally substituted phenyl, pyridyl, morpholino, piperidinyl, or piperazinyl.

ii) R³ is defined according to one of the following groups:

- [(a.)] (a) hydrogen, halogen, QR or QAr¹, wherein Q is a C₁₋₃ alkylidene chain wherein one methylene unit of Q is optionally replaced by -O-, -S-, -NHCO-, or -NR-, and Ar¹ is an optionally substituted 5-6 membered saturated, partially unsaturated, or fully unsaturated ring having 0-2 heteroatoms independently selected from nitrogen, oxygen, or sulfur;
- [(b.)] (b) hydrogen, OH, OCH₃, OCH₂CH₃, NHCOMe, NH₂, NH(C₁₋₄ aliphatic), N(C₁₋₄ aliphatic)₂, O(CH₂)₂morpholin-4-yl, O(CH₂)₂NH₂,

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$O(CH_2)_2NH(C_{1-4}$ aliphatic), $O(CH_2)_2N(C_{1-4}$ aliphatic) $_2$, bromo, chloro, or
 fluoro; or

[(c.)] (c) hydrogen;

iii) R^4 is defined according to one of the following groups:

[(a.)] (a) a 6-membered saturated, partially unsaturated, or aryl ring having 0-3 nitrogens, a 9-10 membered bicyclic aryl ring having 0-2 nitrogens, or a 5 membered heteraryl ring having 2-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein each said ring is optionally substituted with $(ZR^5)_m$;

[(b.)] (b) an optionally substituted ring selected from phenyl, cyclohexyl, naphthyl, pyridyl, pyrimidinyl, triazinyl, thiazolyl, thiadiazolyl, pyrazolyl, isoxazolyl, indazolyl, or benzimidazolyl, wherein said ring is optionally substituted with $(ZR^5)_m$; or

[(c.)] (c) an optionally substituted phenyl group, wherein said phenyl group is optionally substituted with $(ZR^5)_m$;

iv) W^1 , W^2 and W^3 are defined according to one of the following groups:

[(a.)] (a) W^1 is nitrogen or CH, W^2 is nitrogen or $C-(U)_pR^U$, and W^3 is nitrogen or $C-(V)_qR^V$;

[(b.)] (b) W^1 is nitrogen or CH, W^2 is $C-(U)_pR^U$, and W^3 is $C-(V)_qR^V$; or

[(c.)] (c) W^1 is nitrogen or CH and W^2 and W^3 are each CH; and

v) $(U)_pR^U$ and $(V)_qR^V$ groups are defined according to one of the following groups:

[(a.)] (a) hydrogen, halogen, NO_2 , CN , OR , SR or $N(R)_2$, or C_{1-4} aliphatic, optionally substituted with oxo, OR , SR , $N(R)_2$, halogen, NO_2 or CN ;

[(b.)] (b) hydrogen, Me, OH, OMe or $N(R)_2$; or

[(c.)] (c) both $(U)_pR^U$ and $(V)_qR^V$ are hydrogen.

20. (Currently amended) The compound of any one of claims 16, 17, 18 or 19 claim 19, wherein each occurrence of Z is independently a bond or a C_{1-4} alkylidene chain wherein one

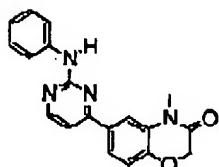
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methylene unit of Z is optionally replaced by -O-, -S-, -SO₂-, or -NH-; and each occurrence of R⁵ is independently hydrogen, C₁₋₆ aliphatic, halogen, NO₂, OR, N(R)₂, or optionally substituted phenyl, pyridyl, and pyrimidinyl.

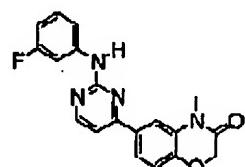
21. (Currently amended) The compound of claim [[19]] 20, wherein each occurrence of ZR⁵ is independently Cl, P, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylene-dioxy methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, aminophenyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

22. (Currently amended) The compound of claim [[1,]] 18 having the formula IVa, wherein R^X is hydrogen or optionally substituted C₁₋₆aliphatic; m is 0, 1 or 2; and ZR¹ is Cl, F, Br, methyl, ethyl, t-butyl, isopropyl, cyclopropyl, nitro, CN, OMe, OEt, CF₃, NH₂, phenyl, benzyl, benzyloxy, OH, methylene-dioxy methylenedioxy, SO₂NH₂, CONH₂, CO₂Me, phenoxy, O-pyridinyl, SO₂phenyl, nitrophenoxy, aminophenoxy, S-dimethylpyrimidine, NHphenyl, NH-methoxyphenyl, pyridinyl, aminophenyl, phenol, chloro-fluoro-phenyl, dimethylaminophenyl, CF₃-phenyl, dimethylphenyl, chlorophenyl, fluorophenyl, methoxyphenoxy, chlorophenoxy, ethoxyphenoxy, or fluorophenoxy.

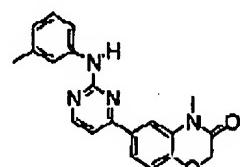
23. (Original) The compound of claim 1, selected from one of the following compounds:



IVa-1

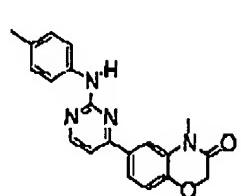


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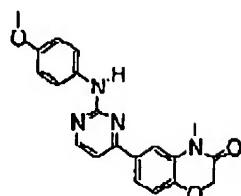


IVa-3

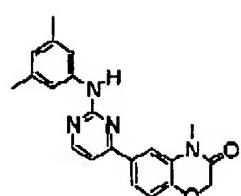
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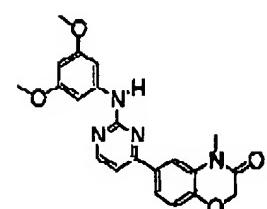
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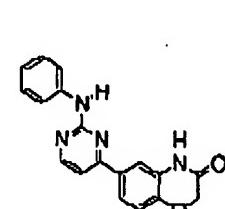
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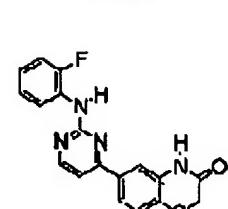
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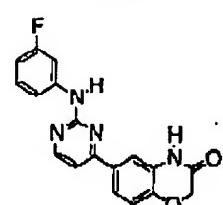
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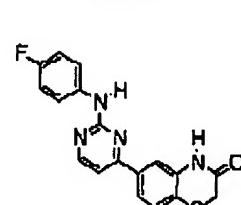
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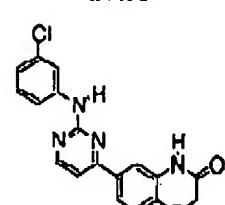
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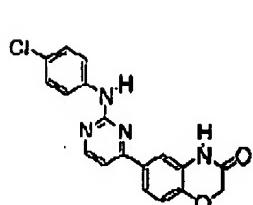
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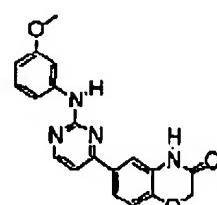
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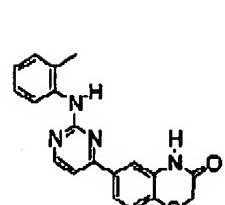
IVa-12



IVa-13

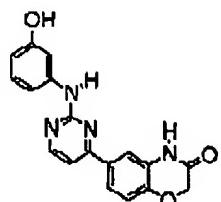


IVa-14

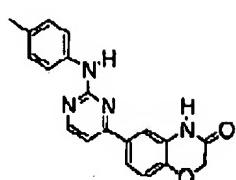


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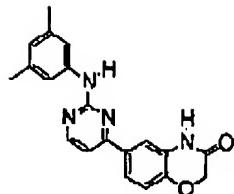
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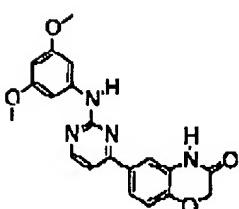
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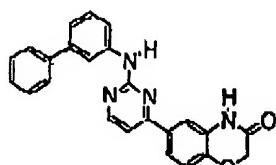
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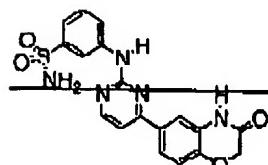
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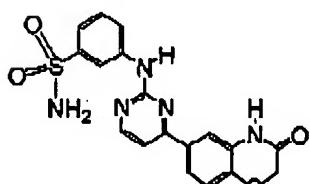
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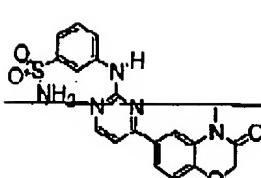
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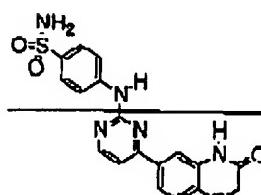
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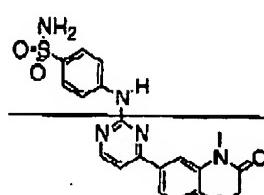
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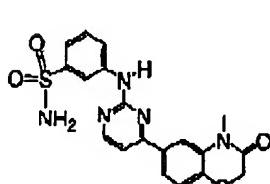
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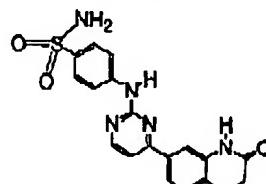
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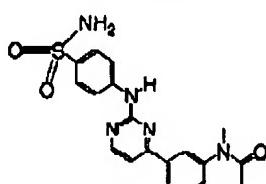
IVa-24



IVa-22

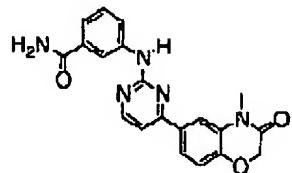


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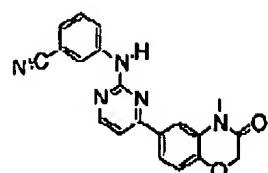


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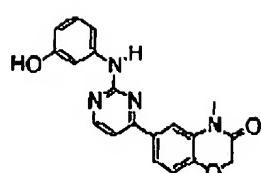
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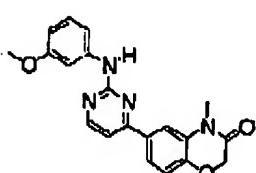
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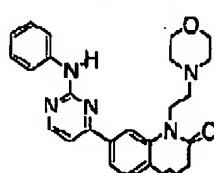
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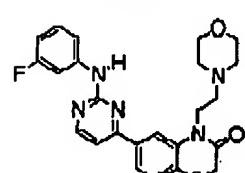
IVa-27



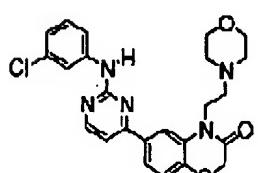
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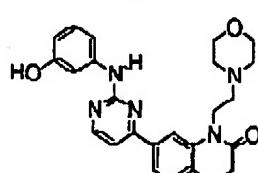
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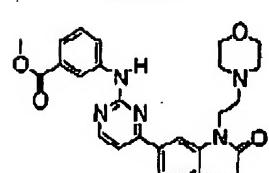
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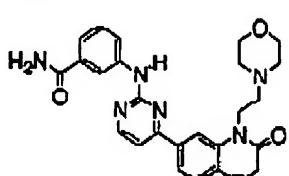
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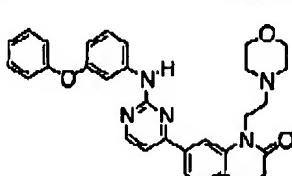
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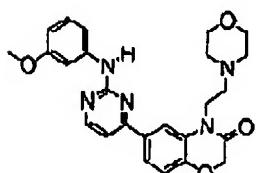
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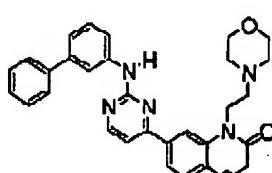
IVa-34



IVa-35

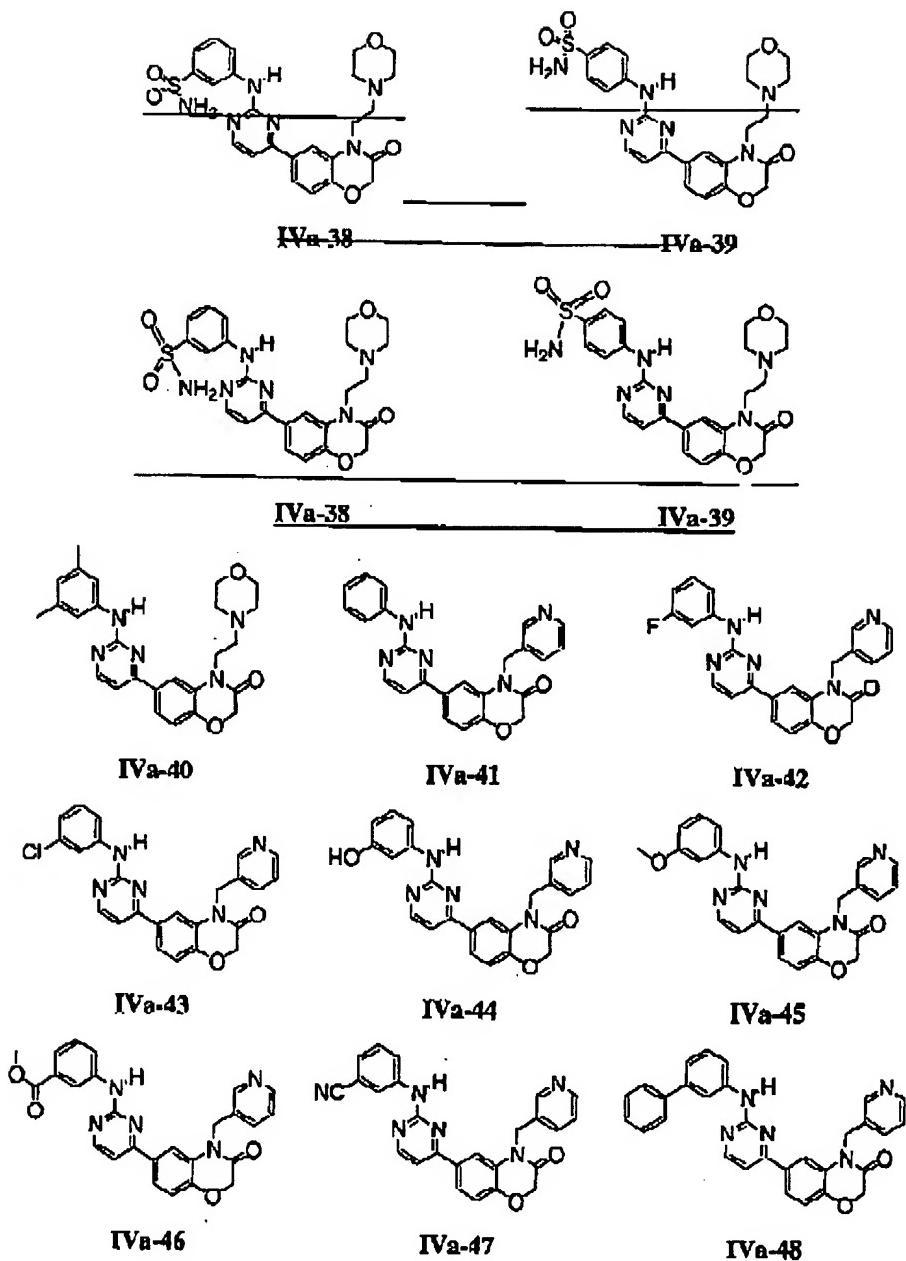


IVa-36

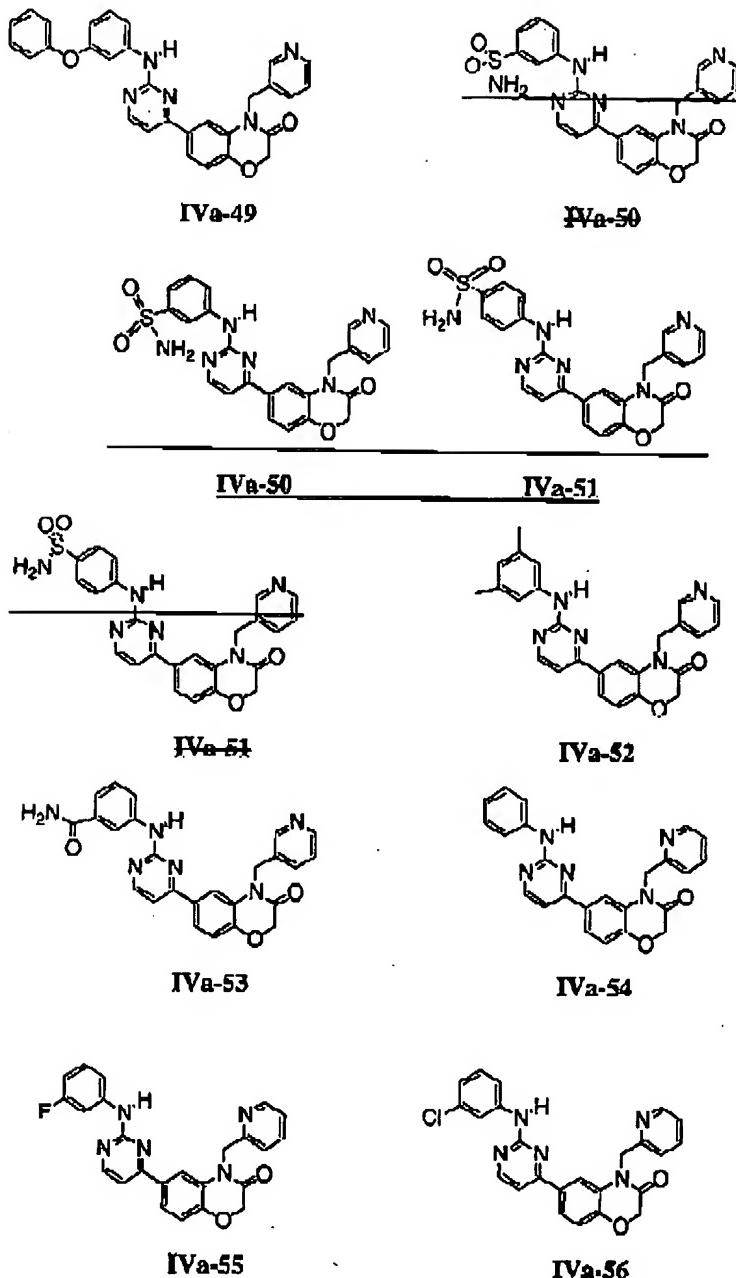


IVa-37

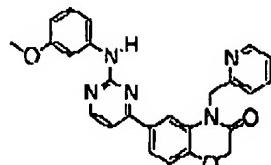
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



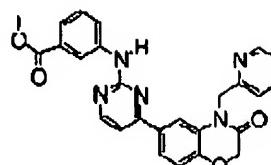
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



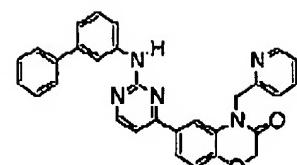
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



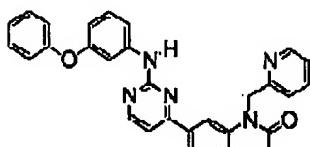
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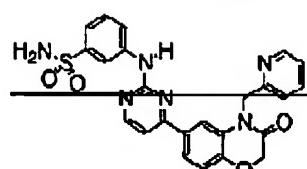
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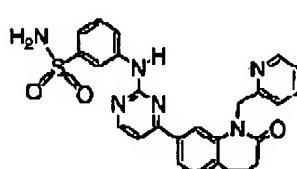
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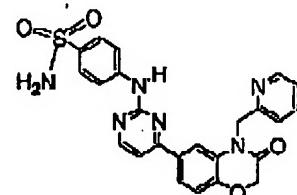
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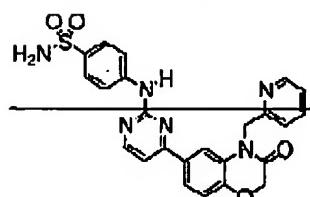
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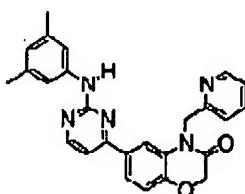
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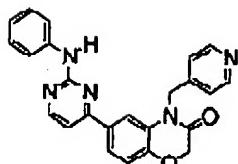
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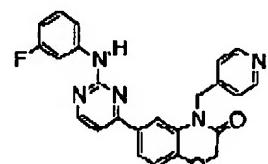
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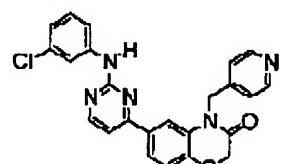
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IVa-64

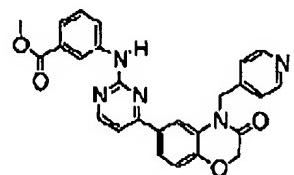


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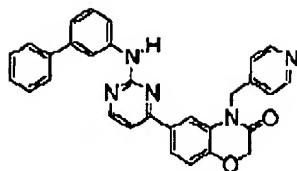


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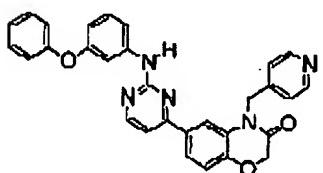
Applicants: Randy S. Bethel et al.
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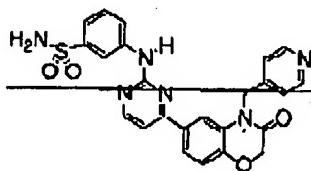
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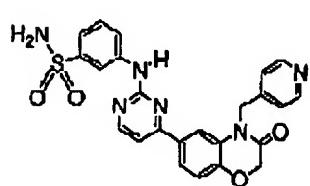
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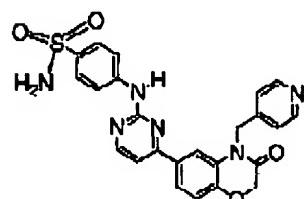
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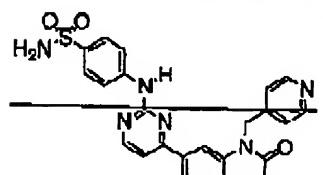
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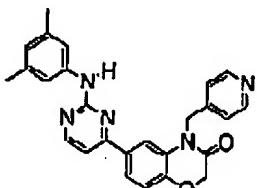
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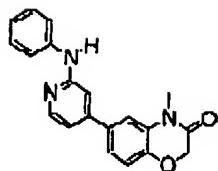
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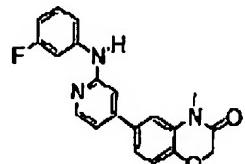
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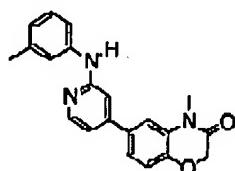
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IVb-1

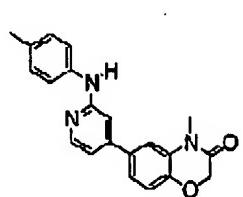


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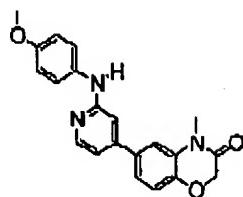


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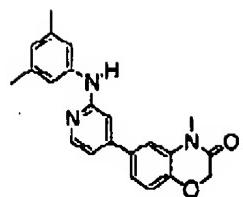
Applicants: Randy S. Bethel et al.
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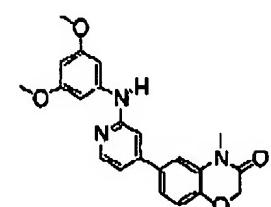
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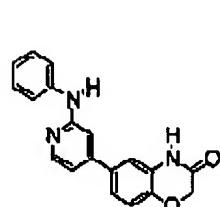
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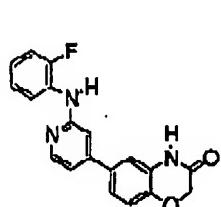
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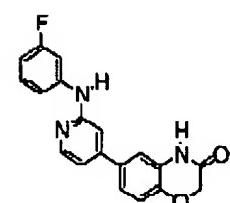
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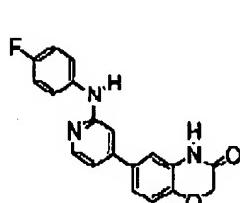
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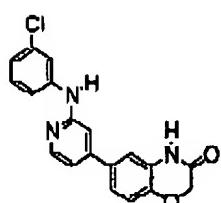
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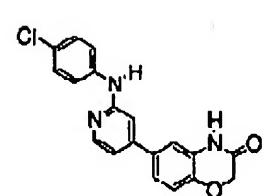
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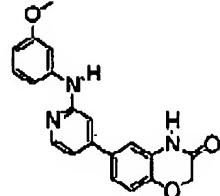
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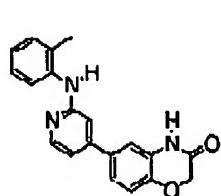
IVb-12



IVb-13

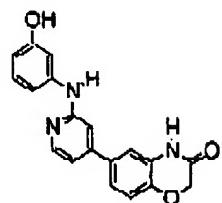


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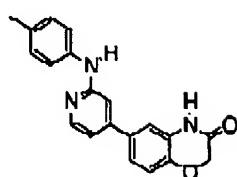


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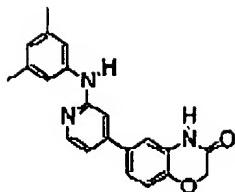
Applicants: Randy S. Bethel et al.
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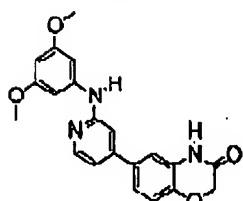
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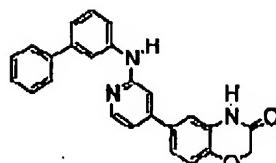
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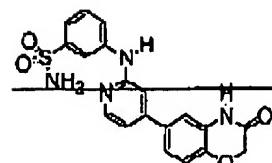
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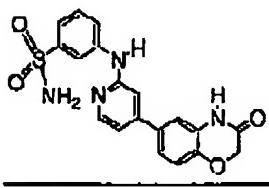
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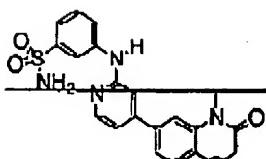
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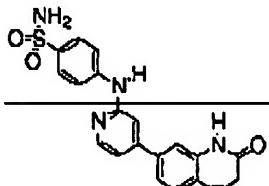
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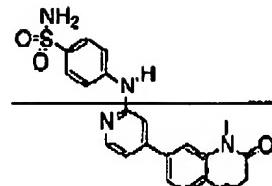
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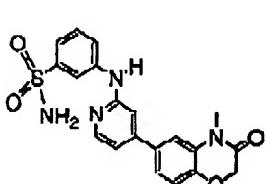
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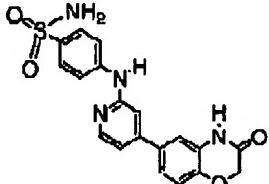
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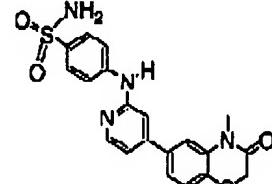
IVb-24



IVb-22

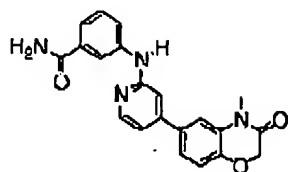


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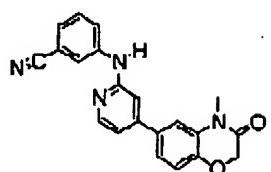


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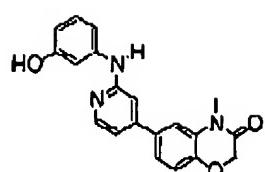
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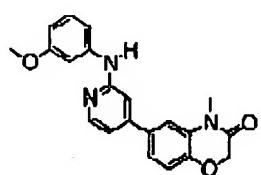
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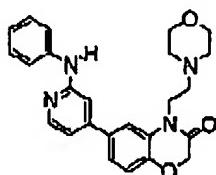
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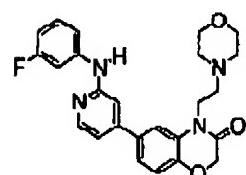
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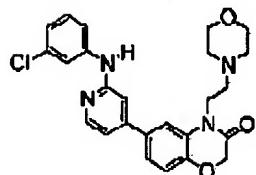
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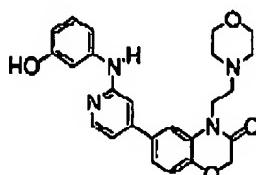
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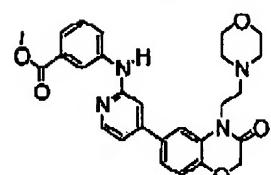
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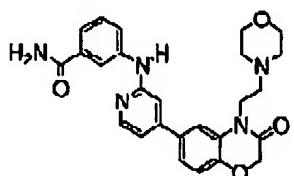
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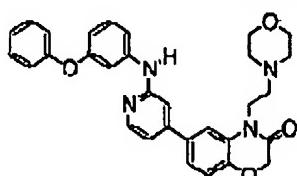
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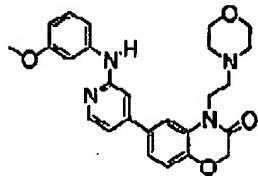
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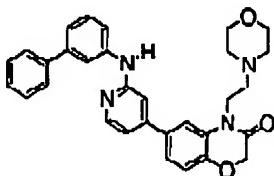
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IVb-35

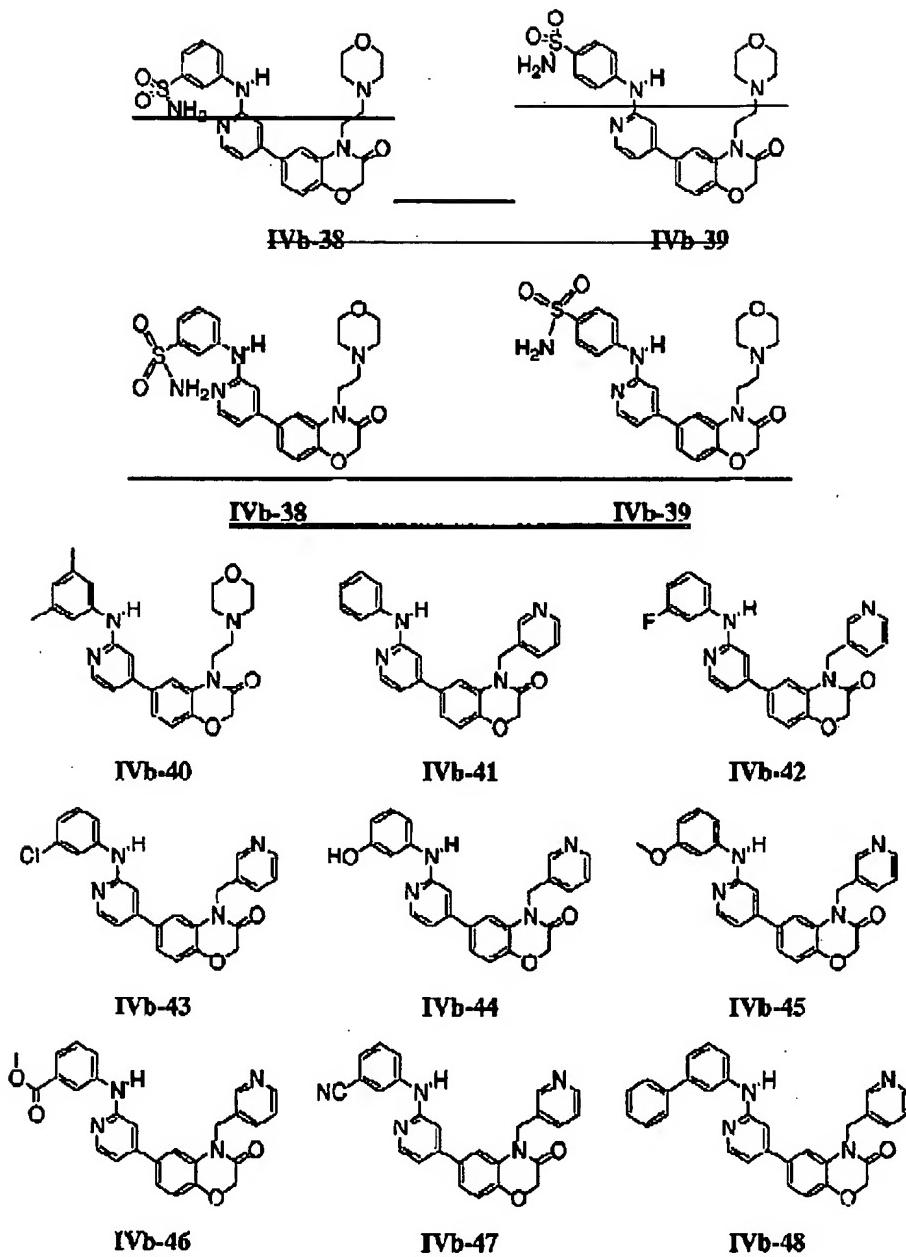


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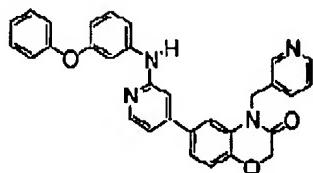


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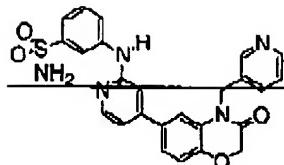
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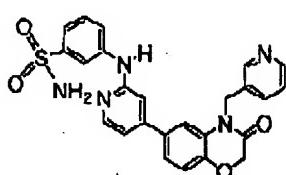
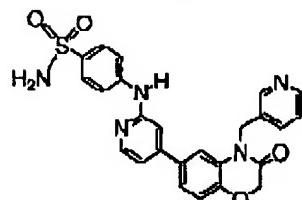
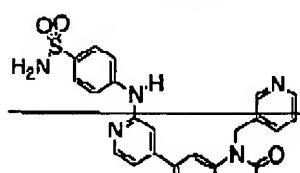
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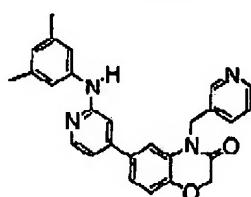
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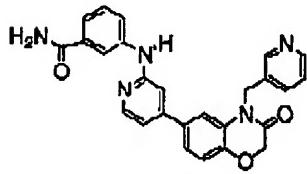
IVb-50

IVb-50IVb-51

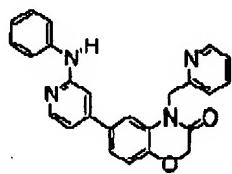
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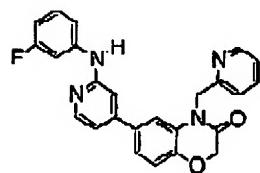
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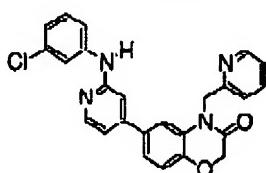
IVb-53



IVb-54

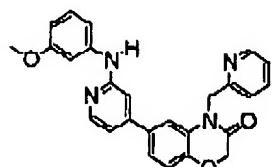


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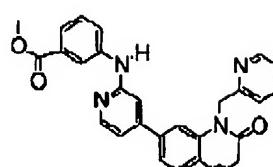


IVb-56

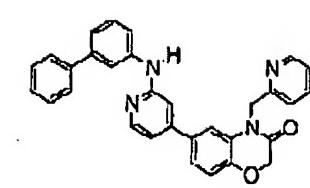
Applicants: Randy S. Bethel et al.
 Application No.: 10/700,936



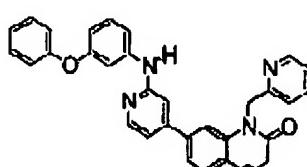
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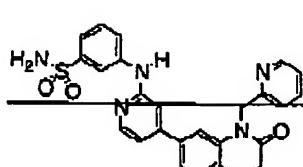
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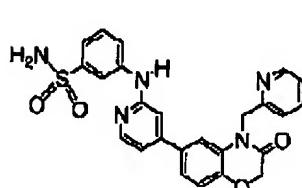
IVb-59



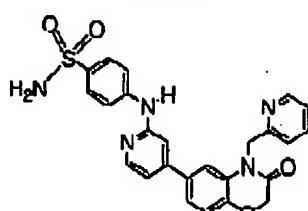
IVb-60



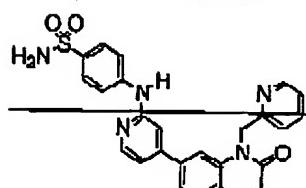
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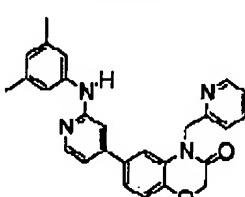
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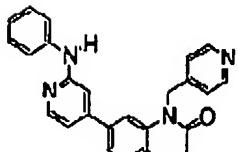
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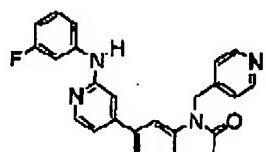
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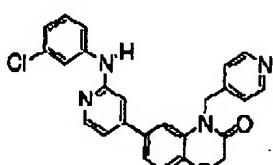
IVb-63



IVb-64

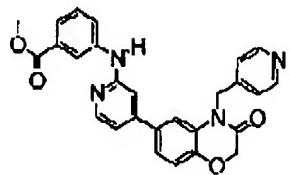


IVb-65

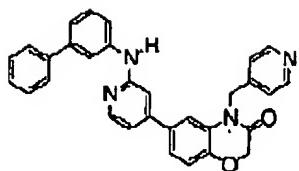


IVb-66

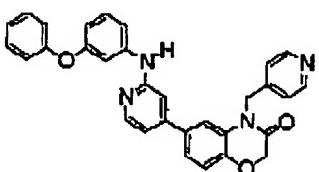
Applicants: Randy S. Bethel et al.
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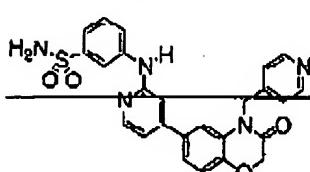
IVb-67



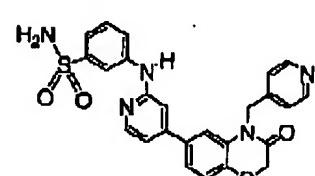
IVb-68



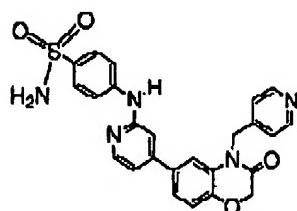
IVb-69



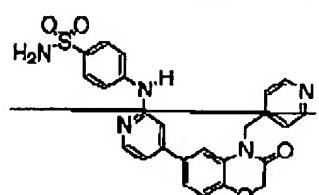
IVb-70



IVb-70

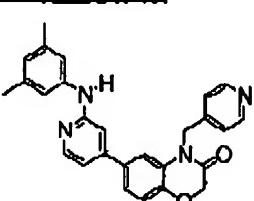


IVb-71



IVb-71

or



IVb-72.

24. (Original) A pharmaceutical composition comprising a compound according to claim 1, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

25. (Canceled)

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26. (Previously presented) A method of inhibiting JAK-3 kinase activity in:

- (a) a patient; or
- (b) a biological sample;

which method comprises administering to said patient, or contacting said biological sample with a compound of claim 1 or a composition comprising said compound.

27. (Previously presented) A method of treating or lessening the severity of a disease or disorder selected from an immune response, an autoimmune disease, a neurodegenerative disease, or a solid or hematologic malignancy comprising administering to a subject in need thereof a compound of claim 1 or a composition comprising said compound.

28. (Original) The method of claim 27, wherein the disease or disorder is selected from an allergic or type I hypersensitivity reaction, asthma, transplant rejection, graft versus host disease, rheumatoid arthritis, amyotrophic lateral sclerosis, multiple sclerosis, Familial amyotrophic lateral sclerosis (FALS), leukemia, or lymphoma.

29. (Original) The method of claim 28, comprising the further step of administering to said patient an additional therapeutic agent selected from a chemotherapeutic or anti-proliferative agent, a treatment for Alzheimer's Disease, a treatment for Parkinson's Disease, an agent for treating Multiple Sclerosis (MS), a treatment for asthma, an agent for treating schizophrenia, an anti-inflammatory agent, an immunomodulatory or immunosuppressive agent, a neurotrophic factor, an agent for treating cardiovascular disease, an agent for treating destructive bone disorders, an agent for treating liver disease, an agent for treating a blood disorder, or an agent for treating an immunodeficiency disorder, wherein:
said additional therapeutic agent is appropriate for the disease being treated; and
said additional therapeutic agent is administered together with said composition as a single dosage form or separately from said composition as part of a multiple dosage form.